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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,683	05/24/2005	Tatsuo Kinashi	2005_0716A	8959

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,683	KINASHI ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *25-27* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4-26-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim 33 has been added. Claims 1-33 are pending.

Election/Restrictions

Applicant's election without traverse of Group V, claims 25-27, in the reply filed on 11-16-07 is acknowledged.

Claims 1-24 and 28-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11-16-07.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 25-27 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

Claims 25-27 are directed toward a transgenic animal having a regulated expression of a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO: 10.

According to the sequence listing of SEQ ID NO: 9, it appears that the amino acid sequence of SEQ ID NO: 10 and the nucleic acid sequence encoding it (SEQ ID NO: 9) is house mouse RAPL (Region 104-901 of mRNA). No other mention of SEQ ID NO: 10 can be found in the specification.

The specification appears to distinguish RAPL and Rapl in the title of the application (Regulation of interaction between RAPL and Rapl). The specification states p30 is equivalent to RAPL (pg 2, line 14-15). Apparently RAPL binds Rapl (pg 1, lines 5-7; "The present invention relates to techniques that allow regulation, e.g. inhibition or promotion, of Rapl-p30 binding" and "The present inventors have succeeded in uncovering that p30 (i.e. RAPL) functions as an effector molecule for Rapl and that p30 is a molecule to positively regulate adhesion and migration by LAF-1"; pg 2, lines 9-12).

Bowen (US Patent Application Publication US 2003/0144196 A1) teaches Regulated in Activated T Lymphocytes (RATL) 5h6 (Example 4, Fig. 12 B), which is 100% homologous to SEQ ID NO: 10 disclosed in the instant application.

Kinashi (WO 2004/040302-A1) teaches human Rapl (regulator for cell adhesion and polarization enriched in lymphoid tissues) (SEQ ID NO: 4), which is 100% homologous to SEQ ID NO: 10 disclosed in the instant application.

Teh (WO 2005/047519-A2) teaches human renal cell carcinoma-related NORE1B protein (SEQ ID NO: 123), which is 100% homologous to SEQ ID NO: 10 disclosed in the instant application.

Walker (US Patent 6,485,910) described a "consensus" cDNA sequence encoding "mammalian" Ras association domain containing protein (RADCP) (SEQ ID NO: 1) (col. 3, lines 16-29), which shares 99.8% identity to SEQ ID NO: 10 disclosed in the instant application.

Walker (US Patent 6,602,667) taught SEQ ID NO: 16, which "is 265 amino acid residues in length and shows about 93% sequence identity from about residue 39 to about residues 265 with Maxp1, a rat protein which interacts with Mss4, a guanine nucleotide exchange factor (g2459833), and about 91% sequence identity from about residue 38 to about residue 265 with. Norel, a mouse putative Ras effector that plays a role in transmitting growth and differentiation signals received from Ras proteins (g2997698). PFAM analysis confirms that SEQ ID NO: 16 from about residue 119 to about residue 211 matches a Ras association domain which interacts directly with the Ras proteins", which shares 99.8% identity with SEQ ID NO: 10 disclosed in the instant application.

Given the lack of teachings in the specification taken with the lack of consensus in the specification regarding the function of SEQ ID NO: 10, the function of SEQ ID NO: 10 was and continues to be unknown.

Pg 67, line 7, states the transgenics are useful for screening inhibitors of the protein. The asserted utility is not substantial because the function of SEQ ID NO: 10 is not disclosed, so it cannot be determined when a compound inhibits SEQ ID NO: 10 from functioning.

Pg 67, line 10, states the transgenics are useful for screening antisense that inhibit the expression of the gene. The asserted utility is not substantial because the specification does not teach how to determine when antisense inhibited SEQ ID NO: 10 expression. Assuming those of skill would be able to determine when antisense inhibited SEQ ID NO: 10 expression, the asserted utility is not substantial because a

transgenic overexpressing SEQ ID NO: 10 is unnecessary – a wild-type mouse expressing normal levels of SEQ ID NO: 10 can be used to determine when antisense inhibits SEQ ID NO: 10 expression.

Pg 67, line 14, states the transgenic animal can be used as a source of cells for tissue culture. The specification states the RAPL (p30) can be analyzed by analyzing DNA, RNA or protein in the tissue. The asserted utility is not specific to the transgenics claimed because the cells can be made by transfection and because the DNA, RNA and protein can be analyzed in cells isolated from a wild type mouse. The asserted utility is not specific because the specification does not teach any assays that are specific to cells isolated from transgenics overexpressing SEQ ID NO: 10. The asserted utility is not substantial because the specification has not provided the blaze marks for those of skill to analyze the DNA, RNA or protein to study the functions of RAPL using cells isolated from the transgenic claimed. Accordingly, the specification has left those of skill to determine how to use cells isolated from the transgenics claimed to determine the function of RAPL.

Pg 67, line 25, states cells isolated from the transgenics can contribute to the development of a pharmaceutical that "enhances functions of various tissues". The asserted utility is not substantial because the function of RAPL binding Rapl was unknown and the function of RAPL in "various tissues" was unknown. Thus, the specification fails to teach how to determine when a compound modulates SEQ ID NO: 10. The specification and the art at the time of filing do not teach one assay to identify compounds that modulate SEQ ID NO: 10. Applicants have left those skilled in the art

with too much "further research" to use the transgenics claimed for identifying compounds that modulate SEQ ID NO: 10. The specification does not teach how to make decisions about the specific controls to use, how to determine when a compound is actually targeting SEQ ID NO: 10 or the gene encoding SEQ ID NO: 10 or how to identify compounds that specifically modulate SEQ ID NO: 10 using cells from the transgenic claimed. Applicants have merely provided a starting point for further research, i.e. making the transgenics, and not provided an end point of a research effort in determining how to use the transgenics or cells of the transgenics to identify compounds that modulate RAPL.

Overall, the mice claimed do not correlate to "research tools" known to have patentable utility. For example, gas chromatographs separate the chemical components of a compound and identify them. Screening assays have various functions, but may be used, for example, to determine the amount of protein expression in a population of cells. Sequencing methods provide the nucleotide sequence of a nucleic acid molecule. Unlike gas chromatographs, screening assays or sequencing methods, the mice claimed are capable of providing data, but the may not reveal the function of the gene or provide any substantially useful information. For example, applicants appear to have made a transgenic mouse expressing RAPL without determining the function of RAPL, correlating overexpression of RAPL to a phenotype of a disease or identifying agents that modulated RAPL function. Further research would be required to determine the function of the RAPL gene, how to use cells isolated from the transgenics or how to identify agents capable of treating disease. The utility

guidelines state using a product for further research is not a "substantial" utility. In this case, applicants do not provide adequate guidance for those of skill to use the transgenics claimed or cells isolated therefrom as a research tool to study the function of RAPL.

Claims 25-27 are also rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 25-27 encompass transgenic humans which are non-statutory subject matter. Please insert "non-human" after "transgenic."

Claim Rejections - 35 USC § 112

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-27 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Indefiniteness

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of what applicants consider "essentially identical to SEQ ID NO: 10" in claim 25 or 26 cannot be determined. It cannot be determined when "essential" features of SEQ ID NO: 10 have been included because the "essential" features are not described in the art or the specification. Accordingly, those of skill would not know when they were infringing on the metes and bounds of the claim. The metes and bounds of a "free floating mass associated with mesentery tissue" in claim 10 are indefinite. It cannot be determined how a mass is free floating and "associated with" mesentery tissue at the same time.

Claim 26 is indefinite because it is unclear how the phrase "wherein a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO: 10" further limits claim 25. Claim 25 already requires the transgenic expresses a polypeptide containing an amino acid sequence identical or essentially identical to the amino acid sequence of SEQ ID NO: 10. It cannot be determined when the protein in claim 26 has been "overexpressed" as compared to the "expression" of the protein in claim 25.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25-27 are rejected under 35 U.S.C. 102(e) as being anticipated by Walker (US Patent 6,485,910 filed July 11, 2000) as supported by Leder (US Patent 5,175,383) and Roses (US Patent 5,767,337), both incorporated into Walker by reference.

Walker taught a consensus cDNA sequence encoding "mammalian" Ras association domain containing protein (RADCP) (SEQ ID NO: 1) (col. 3, lines 16-29), which shares 99.8% identity to SEQ ID NO: 10. Walker taught making a transgenic animal whose genome comprised SEQ ID NO: 10 (col. 19, line 5, through col. 21, line 11) using the techniques for making transgenic rodents described by Leder and Roses. The techniques of Leder and Roses include making a transgenic mouse whose genome comprises a nucleic acid sequence of interest under the control of a regulatory element. Thus, rejection under 102 is proper because Walker incorporates the patents into the specification (col. 32, lines 12-13).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker (US Patent 6,485,910 filed July 11, 2000) in view of Leder (US Patent 5,175,383) and Roses (US Patent 5,767,337).

Walker taught a consensus cDNA sequence encoding "mammalian" Ras association domain containing protein (RADCP) (SEQ ID NO: 1) (col. 3, lines 16-29), which shares 99.8% identity to SEQ ID NO: 10. Walker taught making a transgenic rodent whose genome comprised SEQ ID NO: 10 (col. 19, line 5, through col. 21, line

11; col. 19, lines 60-62). Walker did not specifically disclose making a transgenic mouse encoding SEQ ID NO: 1 having regulated expression.

However, the techniques of Leder and Roses are directed toward making a transgenic mouse whose genome comprises a nucleic acid sequence of interest under the control of a regulatory element.

Thus, it would have been obvious to those of ordinary skill in the art at the time the invention was made to make a transgenic rodent comprising the amino acid sequence of SEQ ID NO: 1 as described by Walker, wherein the transgenic rodent was a mouse whose genome comprised a nucleic acid sequence of interest under the control of a regulatory element as described by Leder and Roses. Those of ordinary skill in the art at the time of filing would have been motivated to make a mouse because Walker points to using the techniques of Leder and Roses which are directed toward making transgenic mice having regulated expression of a protein of interest.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Patent Examiner